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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,803	08/24/2001	Henry Yue	PF-0695-2 CON	3863

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INCYTE CORPORATION
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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,803	YUE ET AL.	
	Examin r	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-16,18,21,24,26,27 and 50-52* is/are pending in the application.

4a) Of the above claim(s) *1,2,9,12-16,18,21,24,26,27 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,10,11,51 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Information Disclosure statement (Paper No. 3) filed on September 24, 2001 has been entered and considered.

2. Applicant's election with traverse of Group II (claims 3-7, 10-11, 51 and 52) is acknowledged. The traversal is on the ground(s) that examining both the groups would not be a serious burden, since search for art relating to one group would result in art relating to the other group. This is not found persuasive because of the following reasons: (i) search for one group not necessarily result in art related to another group (ii) separate classification search is prima facie evidence of burden, (iii) the issues are not the same with respect to 35 U.S.C. 112 and 35 U.S.C. 101 statutes, (iv) separate Art units would examine the two Groups under ordinary circumstances. Hence the restriction requirement is still deemed proper.

3. Claims 8, 17, 19-20, 22-23, 25, and 28-49 are cancelled and claims 1-2, 5, 9-10 and 16 have been amended. New claims 50-52 are added

4. Claims 3-7, 10-11, 51-52 are considered for examination in this office action. Claims 1-2, 9, 12-16, 18, 21, 24, 26-27 are withdrawn from further consideration.

5. This application is a continuation of US application number 09/311,894 filed on May 14, 1999 which is abandoned.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-7, 10-11, and 51-52 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claimed nucleic acids, vectors, host cells, and methods of making and using the nucleic acids are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid. The specification states that the FLEXGEM polynucleotides are useful in the diagnosis, prevention, and treatment of developmental, cell proliferative, and immunological disorders. The specification also teaches DNA sequences which encode FLEXGEM derivatives, or fragments useful in identifying or screening nucleic acid compounds encoding FLEXGE markers, to purify ligands and use as probe

arrays for gene expression. These are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acid being claimed. Further, none of the recited utilities in the specification are specific to the SEQ ID No. 26. None rely on any unique feature of this nucleic acid, SEQ ID NO. 26.

Further, the claimed nucleic acids, vectors, host cells, and methods of making and using the nucleic acids are not supported by a substantial utility because while the specification teaches FLEXGEM encoding polynucleotides could be used in diagnosis, prevention, and treatment of developmental, cell proliferative, and immunological disorders, such diseases comprise a laundry of diseases and disorders which do not make apparent "real world" use for the claimed polynucleotide. No substantial utility has been established for the claimed subject matter for example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly

indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acids have specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, or the laundry list of diseases they could be used to diagnose, prevent, or treat, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

The specification at table 4 teaches that the library from which SEQ ID No. 26 comes- was constructed using RNA from diseased breast tissue. However it does not establish that SEQ ID No. 26 is a marker for breast diseases or even any specific breast disease because the specification also teaches at table 3- that the SEQ ID No. 26 is expressed in various other reproductive, gastrointestinal and nervous tissue. The specification has not established any

correlation between the expression of SEQ ID No. 26 and any specific disease or condition. Further experimentation would be required of the skilled artisan to reasonably confirm a real world use for the claimed polynucleotide and polypeptide it encodes.

As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-7, 10-11, and 51-52 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, the claims are not enabled for making or using a nucleic acid encoding "a biologically active" fragment of SEQ ID NO: 26 or an "immunogenic fragment" of SEQ ID NO: 26 (with regard to claim 3 which depends from 1c and 1d). The specification does not teach the function or biological activity of SEQ ID NO: 6 or any specific amino acid fragments of SEQ ID NO: 6 that would elicit an immune response, for example. Without a teaching of the biological function or activity of SEQ ID NO: 6 or a teaching of where and how to modify the polypeptide to produce a protein with the same or different functionality, the skilled artisan would be unable

to predictably determine what constituted a biologically active or immunogenic fragment of SEQ ID NO: 6, without extensive unpredictable trial and error analysis. While the specification teaches at table 2 that SEQ ID NO: 6 contains potential phosphorylation and glycosylation sites, such recitation does not make clear the specific biological function or activity of SEQ ID NO: 6. Further, the specification does not teach any specific assay to measure the biological activity of SEQ ID NO: 6. While the specification teaches the amino acid sequence of the polypeptide of SEQ ID NO: 6, one sequence does not enable a genus of biologically or immunologically active polypeptide molecules based on the single structure disclosed in the instant application. Therefore, the ordinary artisan would be required to perform undue experimentation to identify any polypeptide, which was an active fragment of the polynucleotide of the presently claimed invention. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for its activity. Such experimentation would be replete with unpredictable trial and error analysis and is considered undue.

8. Claims 3-7, 10-11, 51-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-7, 10-11, 51-52 are drawn to an isolated polynucleotide, fragments comprising of biologically and immunologically active fragments of said polynucleotide, 60 contiguous nucleotides of said polynucleotide, recombinant polynucleotide comprising said polynucleotide,

vectors and transformed cells comprising said recombinant polynucleotide and arrays comprising said polynucleotides.

The specification teaches isolated polynucleotides referred collectively as "full length expressed genetic markers". The specification teaches isolated polynucleotide comprising SEQ ID NO. 26, expression of said polynucleotide in a host cell, and a vector carrying said polynucleotide. The specification defines full-length expressed genetic markers (FLEXGEM) as substantially purified from any species, particularly a mammalian species, any source. The specification further defines allelic variants as an alternate form of the gene encoding FLEXGEM, which may result in one mutation (additions, substitutions of nucleotides) in nucleic acid sequence. The specification also defines biologically active as a naturally occurring molecule having structural, regulatory or biochemical functions. However, the breadth of the claims encompass a large genus of mutants, variants and homologs of SEQ ID NO. 26, from any source, that have not been taught or described by the specification.

The claims are broadly drawn to nucleic acids sequences having at least 90% identity to the nucleotide sequence according to SEQ ID NO.26, biologically active or immunogenic fragments comprising sequence of SEQ ID NO.26, and sequence complementary polynucleotides of said SEQ ID No. 26. Such recitation encompasses an extremely large genus of mutants, variants, and homologs of SEQ ID NO. 26, from any source. The recitation of fragments, complementary sequences and polynucleotide comprising 60 contiguous nucleotides and polynucleotide having at least 90% identity with SEQ ID NO. 26, constitute an extremely large genus, wherein the disclosure of the single sequence of SEQ ID NO.26 is not representative of this large genus. Applicant has expressed possession of only one species in a genus, which comprises hundreds of

millions of different sequences. The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common elements or attributes of the sequences are disclosed. The function of the encoded polypeptide is not disclosed, nor does the specification teach what constitutes a biologically or immunogenic fragment. The specification does not teach or describe which amino acids are critical for any function of the protein sequence of SEQ ID NO. 6. With regard to the fragment or a complementary sequence of SEQ ID No.26, the recitation of the single sequence of SEQ ID No. 26 is insufficient to demonstrate identity of biological activity or function in all of these different species where no structural information regarding where in the sequence the biological activity resides. With regard to a polynucleotide comprising at least 90% sequence identity- such recitation encompasses sequences with the same biological activity as well as sequences with different biological activity of SEQ ID No. 26.However, without a teaching of residues critical for any "biological activity' or 'immunogenic activity' the skilled artisan would be unable to envision the structure of the encompassed mutants, variants and homologs or fragments encoded by SEQ ID NO. 26.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO.26, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 3-7, 10-11, 51-52 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 recites "an isolated polynucleotide comprising a biological fragment / an immunological fragment having sequence of SEQ ID No. 26", which is unclear and indefinite because it is not clear whether a fragment comprising a minimum of one codon of SEQ ID No. 26 constitutes a biologically active / immunogenic fragment or any fragment of any length constitutes a biologically active/ immunogenic fragment.

B. Claims 3-7, 51-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are incomplete for being dependent on non-elected claims. Amendment to recite the claims in an independent format would obviate the rejection.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 6-7, 10-11, are rejected under 35 U.S.C. 102(b) as being anticipated by Ansari-Lari et al. (Genome Res., Vol. 7(3), pages 268-280, 1997).

With reference to Claim 3, and 10, Ansari-Lari et al. teach an isolated polynucleotide comprising a biologically active or immunogenic fragment of SEQ ID No.26 and complementary polynucleotide to the sequence of SEQ ID NO. 26 (see sequence –alignment from GenEmbl database, 100% local similarity with SEQ ID NO. 26). The term 'complementary' has been interpreted to encompass less than the full length complement. With reference to claims 11, Ansari-Lari et al. also teach said polynucleotide comprises at least 60 contiguous nucleotide of SEQ ID No. 26 (see sequence alignment continuity with no gaps). With regard to claims 6-7, Ansari-Lari teaches that the cDNA clones were obtained from M13 library (M13-derived vectors containing the said clones) (see page 277, paragraphs 1-2 of Methods section). Thus the disclosure of Ansari-Lari et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ansari-Lari et al. (Genome Res., Vol. 7(3), pages 268-280, 1997) in view of Brennan (USPN. 5, 474, 796).

Ansari-Lari et al. teach an isolated polynucleotide comprising a biologically active or immunogenic fragment of SEQ ID No.26 and complementary polynucleotide to the sequence of SEQ ID NO. 26 (see sequence –alignment from GenEmbl database, 100% local similarity with SEQ ID NO. 26). The term 'complementary' has been interpreted to encompass less than the full length complement. Ansari-Lari et al. also teach said polynucleotide comprises at least 60 contiguous nucleotide of SEQ ID No. 26 (see sequence alignment continuity with no gaps). However, Ansari-Lari et al. did not teach a microarray comprising at least one said polynucleotide.

Brennan teaches designing and making an array comprising nucleotide sequences bound to a specific site on the array or solid support (see column 2, lines 11-29, column 7, lines 19-67) and is used to detect a target nucleic acid sequence of interest (see column 3, lines 11-22, column 9, example 4).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine polynucleotide elements as taught by Ansari-Lari et al. with the array as taught by Brennan to achieve an expected advantage of developing a high-throughput and sensitive array because Brennan et al. taught that "high density arrays can be used to determine target nucleic acid sequence and aid in screening various ligands , antagonists and agonists of biologically active compounds" (see column 3, lines 11-35). An ordinary practitioner would have been motivated to combine the polynucleotide as taught by Ansari-Lari et al. with the incorporation of the limitation (an array) as taught by Brennan to develop a high-

throughput device for the purpose of screening target nucleic acid samples comprising said polynucleotide, because incorporation of such limitation (array) would enable one skilled artisan to screen a large number of samples at a given time and would result in a cost-effective device.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004 (new tel. # 571-272-0783 effective from 1/9/04). The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 7, 2004

Jehanne S. Sitton
Primary Examiner
Jehanne Sitton
1/7/04